CD5 expression promotes IL-10 production through activation of the MAPK/Erk pathway and upregulation of TRPC1 channels in B lymphocytes

Titre	CD5 expression promotes IL-10 production through activation of the MAPK/Erk pathway and upregulation of TRPC1 channels in B lymphocytes
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Résumé en anglais	CD5 is constitutively expressed on T cells and a subset of mature normal and leukemic B cells in patients with chronic lymphocytic leukemia (CLL). Important functional properties are associated with CD5 expression in B cells, including signal transducer and activator of transcription 3 activation, IL-10 production and the promotion of B-lymphocyte survival and transformation. However, the pathway(s) by which CD5 influences the biology of B cells and its dependence on B-cell receptor (BCR) co-signaling remain unknown. In this study, we show that CD5 expression activates a number of important signaling pathways, including Erk1/2, leading to IL-10 production through a novel pathway independent of BCR engagement. This pathway is dependent on extracellular calcium (Ca) entry facilitated by upregulation of the transient receptor potential channel 1 (TRPC1) protein. We also show that Erk1/2 activation in a subgroup of CLL patients is associated with TRPC1 overexpression. In this subgroup of CLL patients, small inhibitory RNA (siRNA) for CD5 reduces TRPC1 expression. Furthermore, siRNAs for CD5 or for TRPC1 inhibit IL-10 production. These findings provide new insights into the role of CD5 in B-cell biology in health and disease and could pave the way for new treatment strategies for patients with B-CLL.
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